

## Inflammatory Pseudotumour of the Liver Mimicking Cholangiocarcinoma

### Dear Editor,

Inflammatory pseudotumours (IPT) of the liver are rare, benign tumours of uncertain aetiology with great potential for mimicry. We report a case of an IPT occurring on a background of recurrent pyogenic cholangitis (RPC) in a renal transplant recipient. This poses a unique scenario as RPC and long-term immunosuppression pose as risk factors for malignancy and IPT.

### Case Report

A 56-year-old Chinese woman with a history of renal transplant presented with a 2-month history of epigastric discomfort. She was on cyclosporin, prednisolone and azathioprine for her immunosuppression. Clinical examination was unremarkable except for a right lower quadrant scar.

An abdominal ultrasound scan identified a 2 cm x 2.4 cm mass in the left hepatic lobe with associated biliary duct dilatation. Subsequent magnetic resonance imaging (MRI) scan of the liver revealed an atrophic left liver lobe with multiple strictures and distal duct dilatation. There was a 2-cm mass lesion at the origin of the left hepatic duct (Fig. 1).

In view of the underlying RPC, prolonged immunosuppression and radiological features suggestive of a primary hepatic tumour, surgical resection was performed. Intra-operatively, a hard sclerotic mass was palpated in the hilum encasing the left hepatic duct and left

hepatic artery (Fig. 2). Histology of the specimen showed a lesion consistent with IPT of the predominantly hyalinised variety (Fig. 3). The lesion was circumscribed with most areas showing dense hyalinised stroma and scattered histiocytic and lymphocytic inflammation. The Epstein-Bar virus (EBV)-encoded ribonucleic acid (RNA) in situ hybridisation (EBER-ISH) was negative. There were no malignant histological features such as mitoses or atypia.

### Discussion

IPT is a rare, benign lesion characterised by a localised mass with fibrous stroma and chronic inflammatory infiltrate. It is also known as inflammatory myofibroblastic tumour or plasma cell granuloma. The most common site of occurrence is within the lung but it can also be found in the central nervous system, salivary glands, larynx, breast, pancreas, spleen, lymph nodes, skin, bladder and liver.

In cases of IPT of the liver in adults, the male:female ratio has ranged from 1:1 to 3.5:1.<sup>1,2</sup> There is a high incidence of IPT in Asian patients of oriental descent.<sup>1</sup> Often, these lesions are discovered on imaging the liver following non-specific symptoms of fever, abdominal pain and weight loss.<sup>3</sup> They are often misdiagnosed as malignant lesions and resected.

Many theories exist on the pathogenesis of liver IPT including intraparenchymal haemorrhage and necrosis, secondary reaction to an intrahepatic rupture of a biliary

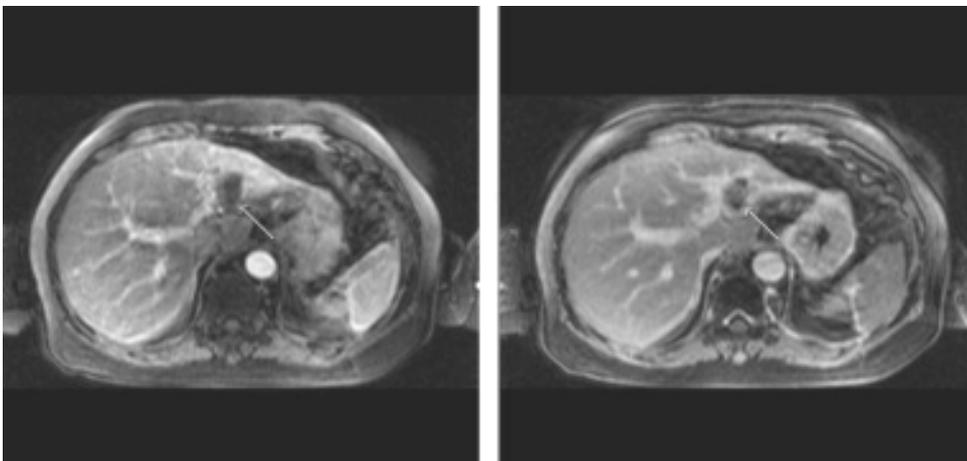


Fig.1. Magnetic resonance scan. Axial fat-suppressed gradient echo T1-weighted 15 minute delayed scan after intravenous gadolinium. The lesion (arrow) shows central progressive enhancement from the early portovenous to equilibrium phases.

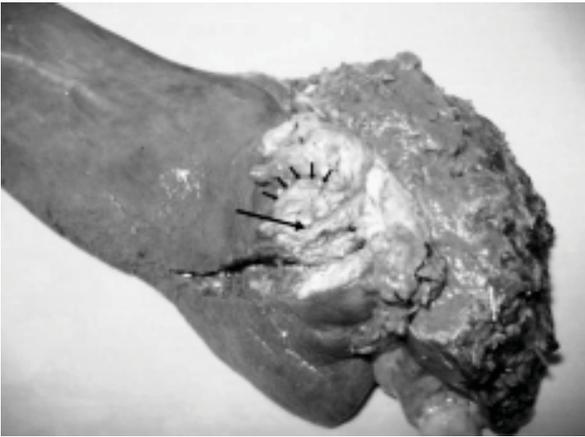


Fig. 2. Resected specimen viewed from posterior aspect. Lesion is indicated by short arrows while bile duct is indicated by solitary long arrow.

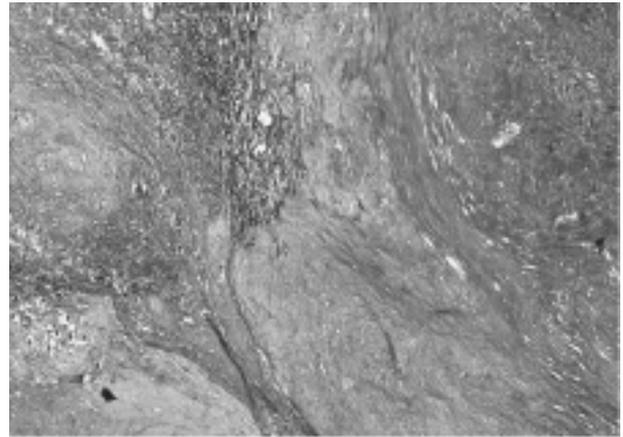


Fig. 3. Masson's trichrome stain. This shows collagenous matrix in green and areas of histiocytes and inflammation in red.

radicle, infection, immune reaction, and occlusive phlebitis of intrahepatic veins. Several previously postulated mechanisms may have contributed to the development of IPT in our patient. First is the presence of chronic suppurative biliary inflammation.<sup>2</sup> Biliary stasis and formation of intraductal stones underlie the chronic recurrent infections of RPC. This can also precipitate ductal necrosis and periductal abscess formation with subsequent formation of IPT with xanthogranulomatous infiltrate. Over a prolonged period, repeated infections and resolution can lead to hyalinised fibrosis. IPT of the liver may represent a spectrum of outcomes in RPC.<sup>1,4</sup>

Second, microorganisms may enter the liver parenchyma through the portal circulation and stimulate an exaggerated inflammatory response.<sup>2,5</sup> Common gram-negative organisms have been isolated from IPT with reports of successful treatment using antibiotics.<sup>6</sup>

Third is the possible link between Epstein-Barr virus (EBV) infection and IPT in the liver.<sup>7</sup> Spindle cells within the IPT showed significantly higher EBV RNA levels. EBV related infections are common in post-transplant recipients on immunosuppression and is suggested to be the causative factor in post-transplant lymphoproliferative disorder. The discovery of IPT of the liver in a transplant recipient can be postulated to be EBV linked.

There is correlation between the degree of fibrosis and cellularity with radiological findings on computed tomography (CT).<sup>4</sup> Areas of fibrosis within the IPT correlate with areas of delayed enhancement; correspondingly areas of high cellular infiltrate are hypodense. This explains why liver IPT has no specific diagnostic features on imaging and may easily mimic other lesions including cholangiocarcinoma.<sup>4,8</sup> Reports of magnetic resonance imaging (MRI) findings

are also non-specific. In our patient, the MRI features for the lesion seen are slight hypointensity on T1-weighted scans, isointensity on T2-weighted images, and central progressive enhancement from the early portovenous to equilibrium phases (Fig. 1). These findings, which are also seen in intrahepatic cholangiocarcinomas, are similar to a previous report.<sup>9</sup>

### Conclusion

In the normal setting, if IPT had been diagnosed on percutaneous needle biopsy, the patient could have been treated non-surgically with antibiotics, anti-inflammatory drugs and steroids.<sup>10</sup> However, in patients with RPC the risk of cholangiocarcinoma is reported to be 4% to 11%.<sup>11</sup> This may be further compounded with post-transplant immunosuppression. Hence, we did not favour the use of percutaneous biopsy in our patient because of the risk of tumour tract seeding. In the setting of RPC, IPT may also coexist with cholangiocarcinoma in the same liver.<sup>4</sup> Furthermore, occult adenocarcinoma in the liver can masquerade as IPT<sup>12</sup> and there have been reports of malignant conversion of liver IPT.<sup>13</sup> These are further arguments against the use of percutaneous biopsy of IPT and subsequent non-operative management. Surgical resection provides both diagnosis and treatment and should be pursued in this setting.

## REFERENCES

1. Shek TW, Ng IO, Chan KW. Inflammatory pseudotumor of the liver. Report of four cases and review of the literature. *Am J Surg Pathol* 1993;17:231-8.
2. Horiuchi R, Uchida T, Kojima T, Shikata T. Inflammatory pseudotumor of the liver. Clinicopathologic study and review of the literature. *Cancer* 1990;65:1583-90.
3. Abbey-Toby A, Cazals-Hatem D, Colombat M, Belghiti J, Vilgrain V, Degott C. Inflammatory pseudo-tumor of the liver: is pre-operative diagnosis possible? *Gastroenterol Clin Biol* 2003;27:883-90.
4. Yoon KH, Ha HK, Lee JS, Suh JH, Kim MH, Kim PN, et al. Inflammatory pseudotumor of the liver in patients with recurrent pyogenic cholangitis: CT-histopathologic correlation. *Radiology* 1999;211:373-9.
5. Lo OS, Poon RT, Lam CM, Fan ST. Inflammatory pseudotumor of the liver in association with a gastrointestinal stromal tumor: a case report. *World J Gastroenterol* 2004;10:1841-3.
6. Torzilli G, Inoue K, Midorikawa Y, Hui AM, Takayama T, Makuuchi M. Inflammatory pseudotumors of the liver: prevalence and clinical impact in surgical patients. *Hepatogastroenterology* 2001;48:1118-23.
7. Arber DA, Weiss LM, Chang KL. Detection of Epstein-Barr Virus in inflammatory pseudotumor. *Semin Diagn Pathol* 1998;15:155-60.
8. Nam KJ, Kang HK, Lim JH. Inflammatory pseudotumor of the liver: CT and sonographic findings. *AJR* 1996;167:485-7.
9. Mortelet KJ, Wiesner W, de Hemptinne B, Elewaut A, Praet M, Ros PR. Multifocal inflammatory pseudotumor of the liver: dynamic gadolinium-enhanced, ferumoxides-enhanced, and mangafodipir trisodium-enhanced MR imaging findings. *Eur Radiol* 2002;12:304-8.
10. Koea JB, Broadhurst GW, Rodgers MS, McCall JL. Inflammatory pseudotumor of the liver: demographics, diagnosis, and the case for nonoperative management. *J Am Coll Surg* 2003;196:226-35.
11. Su CH, Shyr YM, Lui WY, P'Eng FK. Hepatolithiasis associated with cholangiocarcinoma. *Br J Surg* 1997;84:969-73.
12. Schwarz RE, Reynolds JC, Lotze MT. "Pseudo-pseudotumor" of the liver. Adenocarcinoma presenting as an inflammatory pseudotumor. *Dig Dis Sci* 1994;39:2679-84.
13. Pecorella I, Ciardi A, Memeo L, Trombetta G, de Quarto A, de Simone P, et al. Inflammatory pseudotumor of the liver—evidence for malignant transformation. *Pathol Res Pract* 1999;195:115-20.

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